Olema Oncology Announces OP-1250 Demonstrates Attractive Combinability with CDK 4/6 Inhibitor Palbociclib in Phase 1b Dose Escalation Study

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- *OP-1250 in combination with palbociclib was well-tolerated in patients with ER+/HER2- breast cancer, with no dose-limiting toxicities, and no observed drug-drug interaction*
- *No induced metabolism of palbociclib and no safety interaction was observed*
- *Overall tolerability profile of the combination consistent with the FDA-approved label of palbociclib plus an endocrine agent*
- *Phase 2 dose expansion of OP-1250 at 120 mg, the recommended single agent Phase 2 dose, in combination with palbociclib ongoing with additional data to be presented in 2023*

SAN FRANCISCO, Dec. 07, 2022 (GLOBE NEWSWIRE) -- Olema Pharmaceuticals, Inc. ("Olema", "Olema Oncology", or the "Company", Nasdaq: OLMA) today announced results from a Phase 1b dose escalation clinical study of OP-1250, the Company's complete estrogen receptor (ER) antagonist (CERAN) and selective ER degrader (SERD), in combination with palbociclib, a CDK 4/6 inhibitor for the treatment of metastatic ER+/HER2- breast cancer. These results, as of September 12, 2022, were presented today in a poster session at the 2022 San Antonio Breast Cancer Symposium (SABCS) at the Henry B. Gonzalez Convention Center in San Antonio, Texas.

The poster, titled "A Phase 1b/2 dose escalation and dose expansion study of OP-1250, an oral complete estrogen receptor antagonist (CERAN)/selective estrogen receptor degrader (SERD), in combination with the CDK4/6 inhibitor palbociclib in patients with advanced and/or metastatic estrogen receptor (ER)-positive, HER2-negative breast cancer (OP-1250-002; NCT05266105)", highlighted that:

- Across 12 patients, the combination of up to 120 mg of OP-1250 with 125 mg of palbociclib is safe and well-tolerated with no drug-drug interaction (DDI), no induced metabolism of palbociclib, and exposure of OP-1250 in combination with palbociclib is consistent with the observed monotherapy OP-1250 exposure levels.
- There was no dose-related increase in the incidence or severity of adverse events, and neutropenia events observed are consistent with the expected profile of palbociclib plus endocrine therapy.

"OP-1250 continues to demonstrate its potential to be the best-in-class endocrine therapy for ER+/HER2- breast cancer. The results we presented today validate the opportunity to combine OP-1250 with a CDK 4/6 inhibitor for the treatment of metastatic breast cancer," said Sean P. Bohen, M.D., Ph.D., President and Chief Executive Officer of Olema Oncology. "These data show that OP-1250 combines well with palbociclib, including a tolerability profile consistent with palbociclib in combination with an aromatase inhibitor or fulvestrant, no drug-drug interaction, and no induced metabolism of palbociclib. We are actively enrolling our Phase 2 dose expansion at 120 mg of OP-1250 in combination with palbociclib to support a future Phase 3 trial of OP-1250 in combination with a CDK 4/6 inhibitor."

Phase 1b Clinical Results

Enrollment

As of the data cut-off of September 12, 2022, 12 patients with recurrent, locally advanced or metastatic ER+/HER2- breast cancer were treated across four dose escalation cohorts: three patients per cohort dosed at 30, 60, 90, and 120 mg in combination with palbociclib 125 mg. Ten of the 12 patients received prior therapy for advanced disease, including eight patients who had received prior CDK4/6 inhibitors and nine patients who received prior endocrine therapy for advanced disease. Of 11 patients whose circulating tumor DNA (ctDNA) was assessed, 36% had activating mutations in ESR1 at baseline.

Pharmacokinetics

OP-1250 demonstrated favorable pharmacokinetics characterized by high oral bioavailability, dose proportional exposure and a long half-life of eight days, with steady-state plasma levels showing minimal peak-to-trough variability, enabling consistent inhibition of ER for the full dosing interval. There was no observed DDI between palbociclib and OP-1250 in the dose range of 30 mg to 120 mg. Palbociclib did not affect OP-1250 drug exposures compared to monotherapy dosing, and OP-1250 had no effect on palbociclib 125 mg drug exposures when compared to published concentrations.

Safety and Tolerability

Treatment with OP-1250 up to the Recommended Phase 2 Dose (RP2D) of 120 mg was safe and well tolerated with no dose-limiting toxicities, and maximum tolerated dose (MTD) was not reached. The majority of treatment-emergent adverse events (TEAEs) were Grade 1 or 2, and increasing the dose did not show an increase in frequency of events. OP-1250 was not dose-reduced in any patients, and no patients discontinued treatment with OP-1250 due to an adverse event, including

neutropenia. Neutropenia events observed were consistent with the expected profile of palbociclib plus an endocrine therapy. There was no Grade 4 neutropenia, and eight of 12 patients reported Grade 3 neutropenia, a rate which is consistent with the FDA-approved label of palbociclib plus an endocrine agent.

Pre-clinical Combination Study Results

A second poster, titled “Combination of complete estrogen receptor antagonist, OP-1250, and CDK4/6 inhibitors enhances tumor suppression and inhibition of cell cycle-related gene expression”, was presented at SABCS and highlighted pre-clinical data showing that the combination of OP-1250 and CDK4/6 inhibitors, palbociclib and ribociclib, results in greater suppression of transcription related to cell cycle progression than the sum of monotherapies.

Copies of the posters are available on Olema’s website under the Science section.

About Olema Oncology
Olema Oncology is a clinical-stage biopharmaceutical company focused on the discovery, development and commercialization of targeted therapies for women’s cancers. Olema’s lead product candidate, OP-1250, is a proprietary, orally-available small molecule with dual activity as both a complete estrogen receptor (ER) antagonist (CERAN) and a selective ER degrader (SERD). It is currently being evaluated both as a single agent in an ongoing Phase 2 clinical trial, and in combination with CDK 4/6 inhibitors (palbociclib and ribociclib) and a PI3Ka inhibitor (alpelisib), in patients with recurrent, locally advanced or metastatic ER-positive (ER+), human epidermal growth factor receptor 2-negative (HER2-) breast cancer. OP-1250 has been granted FDA Fast Track designation. Olema is headquartered in San Francisco and has operations in Cambridge, Massachusetts.

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